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? s s6 and PY>2003
>>>One or more prefixes are unsupported
>>> or undefined in one or more files.
      64 S6
      13817112 PY>2003
      S7      17 S6 AND PY>2003
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      17 S7
      S8      0 S2 AND S7
? s s4
      S9      178 S4
? s s2
      S10      4 S2
? show files;ds;t/3,k/all
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Set	Items	Description
S1	4	HSV2 (S) ANTISENSE
S2	4	RD (unique items)
S3		
S4	178	S3 AND (MORTALIT? OR FATAL? OR DEATH)
S5	94	RD (unique items)
S6	64	S5 AND PY>2000
S7	17	S6 AND PY>2003
S8	0	S2 AND S7
S9	178	S4
S10	4	S2

>>>KWIC option is not available in file(s): 399

10/3,K/1 (Item 1 from file: 357)  
DIALOG(R)File 357:Derwent Biotech Res.  
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0331276 DBR Accession No.: 2004-03568 PATENT  
**Generating a herpesvirus amplicon particle for treating e.g. cancer,**  
**comprises transfecting a cell with an amplicon plasmid encoding**  
**herpesvirus cleavage/packaging site, herpesvirus origin of DNA**  
**replication and a transgene - virus particle and antisense sequence and**  
**RNA enzyme for use in disease therapy and gene therapy**

AUTHOR: FEDEROFF H J; BOWERS W J  
PATENT ASSIGNEE: UNIV ROCHESTER 2003  
PATENT NUMBER: WO 2003101396 PATENT DATE: 20031211 WPI ACCESSION NO.:  
2004-042969 (200404)

PRIORITY APPLIC. NO.: US 385230 APPLIC. DATE: 20020531  
NATIONAL APPLIC. NO.: WO 2003US17318 APPLIC. DATE: 20030530  
LANGUAGE: English

...ABSTRACT: elements. The cell is further transfected with a sequence encoding a VP16 protein, which is transiently or stably expressed. The VP16 protein is HSV1 VP16, \*HSV2\* VP16, bovine herpesvirus 1 VP16, bovine herpesvirus 1.1 VP 16, gallid herpesvirus 1 VP16, gallid herpesvirus 2 VP16, meleagrid herpesvirus 1 VP16, or equine...

... cos56, and cos48DELTAa. The vectors, individually or collectively, express the structural herpesvirus proteins. The transgene encodes a therapeutic protein or RNA molecule selected from an \*antisense\* RNA molecule, siRNA, or a ribozyme. The therapeutic protein is a receptor, a signaling molecule, a transcription factor, a growth factor, an apoptosis inhibitor, an apoptosis promoter, a DNA replication factor, an enzyme, a structural protein, a neural protein, a histone, an immunomodulatory protein, a tumor-specific antigen, an antigen of an infectious agent, a cytokine or a co-stimulatory molecule. The cytokine is an interleukin, an interferon, or a chemokine. The co-stimulatory molecule is a B7 molecule or CD40L. The tumor-specific antigen is a prostate specific antigen. The infectious agent is a virus or a prion protein, where the virus is a human immunodeficiency virus. The antigen of an infectious agent is gp120, where the infectious agent is a bacterium or parasite. The amplicon plasmid further comprises a promoter. The cell transfected by the method above is a neuron, a blood cell, a hepatocyte, a keratinocyte, a melanocyte, a neuron, a glial cell, an endocrine cell, an epithelial cell, a muscle cell, a prostate cell, a testicular cell, or a germ cell. The cell is preferably a malignant cell. Treating a patient who has or who is at risk for hearing loss comprises administering to the patient an HSV amplicon particle defined above, where the transgene encodes a neurotrophin, specifically neurotrophin-3. The transgene encodes a therapeutic protein that exerts a protective effect on spiral ganglion neurons.

ACTIVITY - Nootropic; Neuroprotective; Cytostatic; MECHANISM OF ACTION - Gene therapy. USE - The HSV amplicon is useful for treating a patient having prion-associated disease (e.g. Creutzfeldt Jacob disease), a patient who has or is at risk for hearing loss, or a patient with cancer or who may develop cancer (claimed) such as lymphocytic leukemia or lymphoma. The HSV amplicon may also be used to treat neurological disorders (e.g. Alzheimer's disease or Parkinson's disease), and disorders resulting in partial or complete loss of hearing.

ADMINISTRATION - The HSV amplicon may be administered directly (e.g. by directing the vector into the tumor), or indirectly by administering cells transduced with the vector to the patient. EXAMPLE - 2 x 10<sup>6</sup> baby hamster kidney cells were seeded on a culture dish, incubated and overnight at 37 degreesC. About 250 microliters of Opti-MEM, 0.4 micrograms of each of 5 cosmid DNAs, and 0.5 micrograms amplicon vector DNA, with or without varying amounts of pBSKS(vhs) plasmid DNA were combined. 10 ml of Lipofectamine Plus (RTM) reagent were added over a 30-second period to the DNA mix, and incubated at room temperature for 20 minutes. In a separate tube, 15 microliters of Lipofectamine Plus (RTM) was mixed with 250 ml Opti-MEM. After incubation, contents of the 2 tubes were combined, incubated for 20 minutes, and the medium in the seeded dish was removed and replaced with the 2 ml Opti-MEM. Transfection mix was added to and incubated at 37 degreesC for 5 hours. Packaging flask was incubated for 3 days more, and virus was harvested and stored until purification. (114 pages)

DIALOG(R)File 357:Derwent Biotech Res.  
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0299276 DBR Accession No.: 2003-01060 PATENT

**Identifying nucleic acid that modulates cell function, or gene expression/biological activity of polypeptide in cell, by double stranded RNA expression libraries/RNA, and post-transcriptional gene silencing techniques - vector expression in human cell, ds RNA expression library use in disease therapy and gene therapy**

AUTHOR: GIORDANO T; PACHUK C; SATISHCHANDRAN C

PATENT ASSIGNEE: NUCLEONICS INC; MESSAGE PHARM INC 2002

PATENT NUMBER: EP 1229134 PATENT DATE: 20020807 WPI ACCESSION NO.:  
2002-610379 (200266)

PRIORITY APPLIC. NO.: US 339260 APPLIC. DATE: 20011026

NATIONAL APPLIC. NO.: EP 2002250681 APPLIC. DATE: 20020131

LANGUAGE: English

...ABSTRACT: immunosorbent assay (ELISA) kit. The HIVgpt cell lines were then used as a model system. Plasmids encoding a 600 nucleotide sense RNA, a 600 nucleotide \*antisense\* RNA and 600 base pair (bp) dsRNA, mapping to the same coordinates of the gag gene of HIV strain HXB2 were used to transfect cells...

... the RNA was from T7 RNA polymerase promoter(s) located at the 5' end of the gag sense strand, at the 5' end to the \*antisense\* strand, or at converging positions at the 5' ends of both the sense and \*antisense\* strands, respectively. Transcription of the RNAs was catalyzed by T7 RNA polymerase, provided from a second co-transfected T7 RNA polymerase expression plasmid. Control plasmids expressing a similar sized sense RNA, \*antisense\* RNA, and dsRNA derived from the gD gene of an herpes simplex virus 2 (\*HSV2\*) genome were included as experimental controls. Cells used were transfected with an expression plasmid encoding a gene product known to interfere with the dsRNA induced...

... RNA polymerase expression plasmid and the gag sense RNA expression plasmid; one well of cells received the T7 RNA polymerase expression plasmid and the gag \*antisense\* RNA expression plasmid; one well of cells received the T7 RNA polymerase expression plasmid and the gag dsRNA expression plasmid; one well of the ...polymerase expression plasmid and the HSVgd sense RNA expression plasmid; one well of the cells received the T7 RNA polymerase expression plasmid and the HSVgd \*antisense\* RNA expression plasmid; and one well of cells received the T7 RNA polymerase expression plasmid and the HSVgd dsDNA expression plasmid. Transfection was again mediated...

... isothiocyanate (FITC) conjugated. None of the gD RNAs specifically shut down p24 synthesis. The double stranded gag RNA significantly down regulated p24. The sense and \*antisense\* had only a modest effect on p24 synthesis, which was predicted to be through the ability of the sense and \*antisense\* gag RNAs to generate low levels of dsRNA species.  
(35 pages)

10/3,K/3 (Item 3 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.

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0286735 DBR Accession No.: 2002-08582 PATENT

**Novel isolated polypeptide comprising at least an immunogenic portion of herpes simplex virus antigen, useful as component of vaccines used for**

**treating herpes simplex virus infection in a patient - vector-mediated  
gene transfer, expression in host cell and antisense oligonucleotide  
for gene therapy**

AUTHOR: HOSKEN N A; DAY C H; DILLON D C; MCGOWAN P; SLEATH P R

PATENT ASSIGNEE: CORIXA CORP 2002

PATENT NUMBER: WO 200202131 PATENT DATE: 20020110 WPI ACCESSION NO.:  
2002-154689 (200220)

PRIORITY APPLIC. NO.: US 277438 APPLIC. DATE: 20010320

NATIONAL APPLIC. NO.: WO 2001US20981 APPLIC. DATE: 20010628

LANGUAGE: English

...ABSTRACT: the expression vectors comprising (II); (5) polynucleotide and polypeptide sequences having substantial identity to the above mentioned sequences; (6) polynucleotides complementary to (II); and (7) \*antisense\* oligonucleotide sequences that specifically bind to (II) or its complement. BIOTECHNOLOGY - Preferred Polypeptide: (I) preferably comprises an immunogenic portion of HSV UL46 (e.g. GlyArgValTyrGluGluIleProTrpValArgValTyrGluAsn, TyrGluAsnIleCysLeuArgArg GlnThrAlaGlyGlyAlaAla, ProAspSerProTyrIleGluAlaGluAsnProLeuTyrAspTrp, TyrIleGluAlaGluAsnProLeuTyrThrTrpGlyGlySerAla, ThrAsnAlaLeuAlaAsnAspGly ProThrAsnValAlaAlaLeu, ArgValLeuProThrArgIleValAlaCysProValAspLeuGly, ThrArgIleValAlaCysProValAspLeuGlyLeuThrHisAla, GluGluIleProTrpValArgVal TyrGlyAsnIleCysProArg, ProGlyThrAlaProAspSerProTyrIleGluAlaGluAsnPro, ProAspSerProTyrIleGluAlaGluAsnProLeuTyrAspTrp, or GluAsnProLeuTyrAspTrp GlyGlySerAlaLeuPheSerPro), HSV UL15 (e.g. SerProAsnThrAspValArgMetTyrSe rGlyLysArgAsnGly, or TyrLeuAlaAlaProThrGlyIleProProAlaPhePheProIle), HSV US3 (e.g. AlaIleAspTyrValHisCysGluGlyIleIleHisArgAspIle), HSV US8A (e.g. AlaPheProValAlaLeuHisAlaValAspAlaProSerGlnPhe) antigen, where the HSV UL46, HSV UL15, HSV US3 or HSV US8A antigens have a 722, 734, 481, or 146 residue amino acid sequence, respectively, all fully defined in the specification. Preferred Fusion Protein: (III) comprises (I) and a fusion partner which: (a) is expression enhancer that increases expression of (III) in a host cell transfected with polypeptide encoding (III); (b) comprises a T helper epitope that is not present within (I); or (c) comprises an affinity tag. Preferred Composition: (VIII) comprises an immunostimulant such as monophosphoryl lipid A, aminoalkyl glucosaminide phosphate saponin, or its combination. Preferred Kit: (IX) comprises (I) immobilized on a solid support, a detection reagent which comprises a reporter group (e.g., radioisotope, fluorescent group, luminescent group, enzyme, biotin or dye particle) conjugated to a binding agent such as an anti-immunoglobulin, protein G, protein A or lectin. Preferred Method: In M1, APC such as dendritic cells, macrophage cells, B cells, fibroblast cells, monocyte cells, and stem cells are incubated with (I). ACTIVITY - Virucide. MECHANISM OF ACTION - Vaccine. No biological data is given. USE - (I) is useful for detecting human immunodeficiency virus (HIV) infection in a patient which involves detecting the presence of antibodies that bind to (I) which is contacted with a biological sample (e.g. whole blood, serum, plasma, saliva, cerebrospinal fluid or urine) obtained from a patient. (I) is also useful for treating HSV infection in a patient which involves incubating peripheral blood cells obtained from the patient in the presence of (I) such that T cells proliferate, and then administering the proliferated T cells to the patient. The T cells are incubated one or more times. Preferably, T cells are separated from the peripheral blood cells obtained from the patient, and incubated in the presence of (I). The obtained T cells are further separated into CD4+ cells or CD8+ T cells from the peripheral blood cells, and are incubated in presence of (I) such that they proliferate. The method further involves separating gamma/delta T lymphocytes from the peripheral blood cells, and proliferating them in the presence of (I). Incubation of the obtained peripheral blood cells further involves

cloning one or more T cells that proliferated in the presence of (I). (V) which is capable of binding (I), is useful for detecting HSV infection in a biological sample which involves detecting in the sample, a polypeptide that binds to (V). (VII) and (VIII) are useful for stimulating immune response in a patient. (All claimed). (II) is useful as probes and primers for nucleic acid hybridization. The probes and primers are useful for detecting HSV infection in a patient. (X) is useful for removing HSV infected cells from a biological sample. The treated biological sample is then used for inhibiting the development of HSV infection in a patient. ADMINISTRATION - Pharmaceutical compositions comprising (I), (II), T cells or (V) are administered by oral, parenteral, intravenous, intranasal or intramuscular route. Dosage of (I) ranges from 25 micro-g-5 mg/kg of host. EXAMPLE - Identification of herpes simplex virus (HSV)-2 antigens was carried out as follows: Lymphocytes were obtained from two types of donors with unknown clinical status, and group B) seropositive donors with well characterized clinical status (viral shedding and anogenital lesion recurrences). Cryopreserved peripheral blood mononuclear cells (PBMCs) or lesion-biopsy lymphocytes were thawed and stimulated in vitro with 1 micro-g/ml HSV-2 antigen. Irradiated autologous PBMC were added as antigen presenting cells for the lesion biopsy lymphocytes only. Recombinant interleukin (IL)-2 was added on days 1 and 4. The cells were harvested, washed and replated in fresh medium containing IL-2 and IL-7 on day 7. Recombinant IL-2 was again added on day 10. The T cells were harvested, washed and restimulated in vitro with HSV-2 antigen plus irradiated autologous PBMC in the same manner on day 14 of culture. The T cell lines were cryopreserved at  $1 \times 10^7$  to the power 7 cells/vial in liquid nitrogen on ... retained the ability to specifically proliferate to HSV-2 gene fragment expression cloning libraries prepared in Escherichia coli. HSV-2 (333) DNA was prepared. The \*HSV2\* -1 library was constructed as follows: DNA fragments were generated by sonicating genomic HSV-2 DNA for 4 seconds. The sonicated DNA was then precipitated...

... of the DNA fragments using T4 DNA ligase. The DNA was phosphorylated using T4 polynucleotide kinase, purified and ligated into the pET17b expression vector. The \*HSV2\*-II library was constructed in similar fashion. The \*HSV2\* -1 library was transformed into E. coli for preparation of glycerol stocks and testing of HSV-2 DNA insert representation. The DNA was transformed into...

... measured using a scintillation counter. ELISA assays were performed on cell supernatants following a standard cytokine-capture ELISA protocol for human IFN-g. From the \*HSV2\*-I library screening with T cells from D104, wells HSV2I-H10 and HSV2I-H12, for which both CPM and IFN-g levels were significantly above background, were scored as positive. The positive wells (HSV2I-H10 and HSV2I-H12) from the initial CD4+T cell screening experiment were grown up again from the master glycerol stock plate. Forty-eight sub-clones from each pool were randomly picked, grown up. The subclones were screened against the AD104 CD4+T cell line. A clone (HSV2I-H10 and HSV2I-H12) from the HSV2I-H12 pool breakdown scored positive. This positive result was verified in second AD104 CD4+T cell assay. An HSV antigen which comprises a 271, 1142, 64, 70, 146, 22, 143, 481, 106, 722, 66, 904, 37, 147, 110, 318, 135, 734, 376, 136, 284, 838, 215, 826, 993, 1113, 1037 or 193 residue amino acid sequence, fully defined in the specification was identified from the positive clones. (157 pages)

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133099118 CA: 133(8)99118u JOURNAL

**Herpes simplex virus type 2 growth and latency reactivation by cocultivation are inhibited with antisense oligonucleotides complementary to the translation initiation site of the large subunit of ribonucleotide reductase (RR1)**

AUTHOR(S): Aurelian, L.; Smith, C. C.

LOCATION: Virology/Immunology Laboratory, Department of Pharmacology and Experimental Therapeutics, School of Medicine, University of Maryland, Baltimore, MD, 21201, USA

JOURNAL: Antisense Nucleic Acid Drug Dev. DATE: 2000 VOLUME: 10

NUMBER: 2 PAGES: 77-85 CODEN: ANADF5 ISSN: 1087-2906 LANGUAGE:

English PUBLISHER: Mary Ann Liebert, Inc.

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S11 17 S7

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